REMARKS

Currently, 7-18 are pending. Claims 11-18 have been added. Support for such claims may be found throughout the specification, including, for example, paragraph [0131]. Claims 1-6 have been canceled. Applicant addresses each of the rejections set forth in the Final Office Action in the order presented, as set forth below.

Double Patenting

The Examiner has provisionally rejected claims 7-8 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 4, 5 and 7 of copending U.S. Application No. 10/617,949. Applicant submits herewith a terminal disclaimer, rendering this rejection moot.

35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 7-10 under 35 U.S.C. § 112, first paragraph as failing to comply with the written description requirement. The Examiner alleges that the term "pharmaceutically" acceptable carrier in claims 7-8 does not have express support in the specification and claims as originally filed. While respectfully disagreeing with the Examiner's position because the specification clearly provides support for the use of such compounds as drugs, Applicant has amended claims 7 and 8 to remove the term "pharmaceutically" and to expressly claim a drug, such that the drug comprises a 2-imidazolyl disulfide and an acceptable carrier.

The Examiner also alleges that the compound 1-methylpropyl 2-imidazolyl disulfide does not have support in the specification and claims as originally filed. This is simply not true. As Oblong was incorporated by reference in its entirety, paragraph [0131] has been amended to specifically recite 1-methylpropyl 2-imidazolyl disulfide (See MPEP 2163.07(b)). The compound 1-methylpropyl 2-imidazolyl disulfide is precisely the compound described in paragraph [0131] and is itself set forth in the Oblong reference, which is cited in, for example, paragraph [0131] of the present specification. Accordingly, Applicant has provided adequate written description of such compound.

35 U.S.C. § 102(b)

The Examiner has rejected claims 7-10 under 35 U.S.C. § 102(b) as being anticipated by Oblong et al. Applicant respectfully disagrees.

Oblong describes 1-methylpropyl 2-imidazolyl disulfide among a number of asymmetric disulfides, and not until the present application is it appreciated that 1-methylpropyl 2-imidazolyl disulfide is a drug because it inhibits thioredoxin, as opposed to thioredoxin reductase. Applicant has amended claims 7 and 8 to recite that the drug comprises a 2-imidazolyl disulfide and an acceptable carrier. As set forth in the present application, Applicant unexpectedly found that certain asymmetric disulfides, including in particular 1-methylpropyl 2-imidazolyl disulfide, behaved as a substrate of thioredoxin reductase or inhibitor of thioredoxin. Despite the similarities in structure of asymmetric disulfides and reported *in vitro* inhibitory activities, it was found that 1-methylpropyl 2-imidazolyl disulfide is, in fact, an inhibitor of thioredoxin, irreversibly binding to Cys^{73} and thus a suitable inhibitor of the thioredoxin reductase/thioredoxin system. Applicant unexpectedly found that certain 2-imidazolyl disulfides irreversibly bind to Cys^{73} of thioredoxin and block its reduction by thioredoxin reductase. Other 2-imidazolyl disulfides did not effectively inhibit thioredoxin. This is described in Applicant's later published paper entitled "*Thioredoxin redox signaling: a novel target for anti-cancer drug development*" 7(3) ANTI-CANCER DRUGS 121-26 (1996), which is provided for the Examiner's convenient reference as *Exhibit A*.

Oblong describes 1-methylpropyl 2-imidazolyl disulfide (also referred to in the literature as IV-2) and other asymmetric disulfide compounds as competitive inhibitors with DTNB for reduction by thioredoxin reductase, with III-2, IV-2, and VII-2 having Ki of 3.3, 13.0 and 8.6 μM respectively, and IC_{50} values of Swiss 3T3 murine fibroblasts of 2.0, 3.5 and 4.0 μM respectively (see Figure 2 of Oblong).

Even assuming arguendo that the art suggested that some 2-imidazolyl disulfides may be of interest because they compete with DTNB for thioredoxin reductase, until Applicants' discovery that some asymmetric disulfides in the series irreversibly bind to Cys^{73} of thioredoxin (i.e., they are inhibitors of thioredoxin instead of substrates of thioredoxin reductase), their suitability as therapeutic agents was wishful thinking at best. Further, this unexpected discovery provides one with the ability of determining an effective amount of 2-imidazolyl disulfide in order to reduce or eliminate thioredoxin-associated apoptosis inhibition or inhibit thioredoxin stimulated cell growth. Oblong failed to appreciate that 2-imidazolyl disulfides irreversibly bind to Cys^{73} of thioredoxin, and therefore fails to teach that 1-methylpropyl 2-imidazolyl disulfide as a drug that would be useful for reducing or eliminating thioredoxin-associated apoptosis

inhibition or inhibiting thioredoxin stimulated cell growth. Accordingly, Oblong fails to anticipate claims of the present invention, and this rejection should be withdrawn.

CONCLUSION

Applicant has timely filed this response. In the event that an additional fee is required for this response, the Commissioner is hereby authorized to charge such fees to Deposit Account No. 50-0436.

Should the Examiner have any questions or comments, or need any additional information from Applicant's attorney, he is invited to contact the undersigned at his convenience.

Respectfully submitted,

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